



**UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office**

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

11

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/040,518	03/17/98	KARATZAS	C 06632/011001

PAUL T CLARK
CLARK EBING
176 FEDERAL STREET
BOSTON MA 02110

HM12/0104

EXAMINER

BAKER, A

ART UNIT

PAPER NUMBER

1632

DATE MAILED:

14
01/04/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/040,518

Applicant(s)

KARATZAS ET AL.

Examiner

Anne M. Baker

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 October 2000.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 and 7-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 7-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

Application/Control Number: 09/040,518

Page 2

Art Unit: 1632

DETAILED ACTION

The amendment filed October 16, 2000 (Paper No. 13) has been entered. Claims 2, 3, 5, 13, and 14 have been amended. Claim 6 has been cancelled.

Claims 1-5 and 7-21 are pending in the instant application.

The following rejections are reiterated or newly applied and constitute the complete set of rejections being applied to the instant application. Rejections and objections not reiterated from the previous office action are hereby withdrawn.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 2 stands rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The claimed invention is not supported by either a specific asserted utility or a well-established utility.

The claim is drawn to a non-human mammalian embryo comprising a cell whose nucleus comprises a nucleic acid molecule encoding a biofilament operably linked to a promoter and leader sequence that direct expression of the biofilament in milk-producing cells or urine-producing cells.

Neither the specification as filed nor any art of record discloses or suggests any specific use for the claimed mammalian embryo. As the embryo does not secrete milk or excrete urine, the embryo cannot be used to produce biofilaments.

Art Unit: 1632

No specific asserted utility or well-established utility is disclosed for the mammalian embryo harboring the recited construct.

Note that, because the claimed invention is not supported by a specific asserted utility as set forth above, credibility cannot be assessed.

Applicants argue that the embryo can be used to create an adult transgenic animal that has utility. However, the embryos are merely intermediates formed in producing a transgenic animal that has utility, but the embryos do not themselves have a utility.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 2 stands rejected under 35 U.S.C. 112, first paragraph, for reasons of record advanced on page 3 of the previous Office Action mailed 4/12/00 (Paper No. 11). Specifically, since the claimed invention is not supported by either a specific asserted utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicants again argue that the claimed embryo has utility and that one skilled in the art would know that the embryo can be used to generate an adult animal from which secreted biofilaments may be obtained. This argument has already been addressed herein above.

Claims 1 and 3-21 stand rejected under 35 U.S.C. 112, first paragraph, for reasons of record advanced on pages 4-7 of the previous Office Action mailed 4/12/00 (Paper No. 11), as containing subject

Art Unit: 1632

matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants argue that any experimentation required to make the claimed transgenic animals would not be considered undue because the specification provides ample guidance for producing the necessary constructs required to make the transgenic animals and the specification provides guidance with regard to a protocol that is generally applicable for generating transgenic animals that express a biofilament in their milk or urine. While the specification provides specific teachings with regard to constructs that could be used to produce transgenic animals, the specification does not provide adequate guidance for producing the claimed transgenic animals. Since the transgenic animal art is inherently unpredictable, as discussed in the previous Office Action, general guidelines are not sufficient to teach the skilled artisan how to make the claimed animals. The level of expression of the transgene in specific tissues is crucial to the operability of the invention. As discussed previously, numerous parameters must be taken into consideration to achieve the desired level of tissue specific expression. The effect of a particular transgene construct on the phenotype of a transgenic animal cannot be predicted. Given the unpredictability in the art, specific guidance is required to practice the full scope of the invention without undue experimentation.

Applicants argue that the level of skill in the art is high and that the teachings in the specification can easily be transferred to other nucleic acid constructs and animals. Applicants further argue that even if a procedure described in the specification would not achieve production of a biofilament in every conceivable animal, this would not negate enablement of the present claims. However, given the unpredictability in the transgenic art, specific guidance must be provided to enable the claimed invention, but the specification does not teach how to make any transgenic animal that produces a biofilament in the milk or urine. Since not even

Art Unit: 1632

a single transgenic animal has been enabled, routine experimentation could not be used to produce other similar transgenic animals.

Applicants argue that the specification need not contain a working example if the invention is otherwise disclosed in such a manner that one skilled in the art is able to practice it without undue experimentation. However, given the unpredictability in the transgenic art, general teachings, guidelines, or protocols are not sufficient to teach the skilled artisan how to make the claimed invention without undue experimentation. Specific guidance is required in an unpredictable art such as transgenic technology. The *in vivo* effect of particular transgene constructs cannot be predicted.

Applicants argue that others have produced transgenic animals that produce a protein in the milk or urine. However, such animals were produced through intensive effort, not routine experimentation. As research is required to determine the *in vivo* effect of various transgenes constructs, this does not constitute routine experimentation. That others have successfully produced transgenic animals that produce a protein in the milk or urine does not obviate the need for further experimentation when new proteins are desired to be produced in similar fashion. Given the unpredictability in the art, this further experimentation rises to the level of undue experimentation, as research is required to come up with appropriate constructs that work in the manner intended for a particular animal species.

Applicants argue that the quantity of experimentation is not undue because the monoclonal antibody screening of *In re Wands* was judged to be routine, not undue. However, hybridoma screening requires the repetitive performance of a defined assay method. In the instant case, research is required to find appropriate constructs that function in the manner intended. Applicants teach only what is intended to be done and how it is intended to work, but do not actually teach how to do that which is intended.

Art Unit: 1632

Applicants assert that transgenic animal technology is predictable. Applicants argue that the reference of Wall, rather than teaching unpredictability as described by the Examiner, actually demonstrates that the state of the transgenic art at the time of filing was such that transgene expression was predictable among various species of mammals. Applicants point to Table 1 of Wall (1996) for demonstrating that “transgene efficiency ranges from 1% in farm animals (cattle, sheep, pigs) to 3% in laboratory animals.” However, this table actually describes transgene integration efficiencies, but says nothing about expression of the transgene once integrated. It is the effect of the transgene that is unpredictable.

With regard to Claims 13 and 15-21, Applicants argue that the claimed method for making transgenic animals of any species is enabled because Applicants have amended Claim 13 to recite that the embryonal cell is transformed rather than transfected. However, as the specification itself clearly defines an “embryonal cell” as a cell that is capable of being a progenitor to all the somatic and germ-line cells of an organism, the claim clearly covers the use of embryonic stem cells. Embryonic stem cell technology is enabled only for mice, as discussed in the previous Office Action.

With regard to Claims 13-21, Applicants argue that the claims have been amended to indicate that the biofilament is expressed and secreted from milk-producing or urine-producing cells. This aspect of the enablement rejection, as advanced on page 7, paragraph 2, is therefore withdrawn.

Claims 2-6 stand rejected under 35 U.S.C., first paragraph, for reasons of record advanced on pages 7-8 of the previous Office Action mailed 4/12/00 (Paper No. 11), as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants are referred to the

Art Unit: 1632

revised interim guidelines on written description published December 21, 1999 in the Federal Register at Volume 64, Number 244, pp. 71427-71440 (also available at www.uspto.gov).

Applicants argue that the claims have been amended to recite a phenotype for the claimed transgenic animals, and thus, the claims recite relevant identifying characteristics for the transgenic animals, and satisfies the written description requirement. However, Applicants have not described a transgenic animal having the phenotype recited in the claims. Thus, Applicants have not convincingly demonstrated that they were in possession of the claimed animals at the time of filing. No animal of the type claimed is disclosed. No transgenic animals have been described by their complete structure. The written description requirement is not satisfied for the claimed genus.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is indefinite in its recitation of "said animal" because the phrase lacks antecedent basis. As amended, Claim 5 is directed to a mammal, not an animal.

Claim 13 is indefinite in its recitation of "a biofilament encoding a nucleic acid molecule" because a biofilament is a protein and cannot encode a nucleic acid.

Claim 13 is indefinite in its recitation of "a milk-producing or urine-producing cell derived from said transformed embryonal cell" because neither milk-producing cells nor urine-producing cells can be derived from an embryonal cell alone.

Art Unit: 1632

Conclusion

No claim is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Baker whose telephone number is (703) 306-9155. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached on (703) 305-6608. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-8724.

Questions of formal matters can be directed to the patent analyst, Kay Pinkney, whose telephone number is (703) 305-3553.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Anne-Marie Baker, Ph.D.

Scott D. Priebe
SCOTT D. PRIEBE, PH.D.
PRIMARY EXAMINER